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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/708,991	04/06/2004	Roberta Nora Malone Rooney		2990

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EXAMINER	
ISSAC, ROY P	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/708,991	ROONEY, ROBERTA NORA MALONE	
	Examiner	Art Unit	
	Roy P. Issac	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application was filed on 06 April 2004. This application does not claim priority to any other applications.

Claim Objections

Claim 16 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claims 2-4 are objected to because of the following informalities: The recitation "disorders: amyotrophic lateral sclerosis" does not make it clear whether the disorders treated are limited to those listed in the claim or open to other disorders as well. A list of transitional phrases and the concise meanings of those phrases can be found in MPEP § 2111.03. Applicant is advised to consider commonly used transitional phrase, "consisting of"

Appropriate correction is required.

Claims 3-4 are objected to because of the following informalities: The recitation, "(amyotrophic lateral scleorsis)" makes the claim scope unclear. Claim 3 depends form claim 2, which recites multiple diseases. It is not clear if claim 3 is limited to amyotrophic lateral sclerosis. As discussed above applicant is advised to consider the above-mentioned transitional phrases.

Appropriate correction is required.

Claims 5-7 are objected to because of the following informalities: Claim 5 recites three diseases in brackets at the end of the claim. It is not clear if claim 5 is limited to the three listed central nervous system disorders or if it encompasses other disorders as well. As discussed above applicant is advised to consider the above-mentioned transitional phrases.

Appropriate correction is required.

Claims 4, 7 and 10 are objected to because of the following informalities: Claims 4 and 7 includes the term "olfactory (nasal)" in reference to olfactory. The term olfactory is defined as "relating to, or contributing to the sense of smell." It is not clear how the applicant intents to modify or the meaning of the term olfactory.

Appropriate correction is required.

Claims 11-13 are objected to because of the following informalities: Claim 11 recites three diseases in brackets at the end of the claim. It is not clear if claim 11 is limited to the three listed central nervous system disorders or if it encompasses other disorders as well. As discussed above applicant is advised to consider the above-mentioned transitional phrases.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-15 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-15 are directed to a method of treatment for common neurological disorders, said method comprising the use of uroporphyrin as a neuroprotector. The specification fails to disclose any use of uroporphyrin to treat any particular diseases. There is no evidence, other than a theory, to suggest that any of the neurological diseases can be treated successfully with uroporphyrin. Applicant asserts in the specification that uroporphyrin I is a neuroprotector and is present in low levels in those suffering from hereditary biochemical multiple sclerosis (HBMS). However, there is no evidence presented, other than a theory, to support this contention. Furthermore, there is no evidence presented to show that the administration of uroporphyrin will ameliorate or remedy any shortcomings in the heme synthesis pathway. One of skill in the art will not regard the applicants to have had possession of the invention in the full scope as claimed in claims 1-15 that encompass the use of

uroporphyrin to treat a series of neurological disorders. The issue is regarding whether the inventor had possession of a broader, more generic invention. See, e.g., PIN /NIP, Inc. v. Platte Chem. Co., 304 F.3d 1235, 1248, 64 USPQ2d 1344, 1353 (Fed. Cir. 2002).

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The record contains no clear and convincing evidence in support of enablement of the instant claimed methods. First, there are no examples, *in vitro* or *in vivo*, showing any particular uorporphyrin molecule having activity towards any of the neurodegenerative diseases claimed.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence

or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The instant invention pertains to a method of treating neurological disorders by the administration of uroporphyrins. This invention relates generally to the treatment of central nervous system (CNS) and peripheral nervous system (PNS) neuropathies, especially amyotrophic lateral sclerosis (ALS), wherein the neurotoxicity associated with the porphyrin precursors, delta-aminolevulinic acid (ALA) and porphobilinogen (PBG), is a contributing factor, and more particularly, to the use of a uroporphyrin isomer, uroporphyrin I (URO I) or uroporphyrin III (URO III) or any of their substrates as such treatment.

The relative skill of those in the art:

The relative skill of those in the art is high, with a typical practitioner having obtained a PhD, M.D. or equivalent advanced degree.

The breadth of the claims:

The claims are deemed very broad because the claims cover the treatment of a broad spectrum of diseases including amyotrophic lateral sclerosis (ALS), stroke, encephalitis, meningitis, acute immunodeficiency syndrome related neuropathy, diabetic neuropathy and Guillaine-Barre syndrome.

The state of the prior art and the predictability or lack thereof in the art:

The porphyrias are a group of disorders due to abnormalities in the pathway of biosynthesis of heme; they can be genetic or acquired. They are not prevalent, but it is important to consider them in certain circumstances (eg, in the differential diagnosis of abdominal pain and of a variety of neuropsychiatric findings); otherwise, patients will be subjected to inappropriate treatments. (Murray et. al., Harper's illustrated biochemistry, Pages 270-285, Page 274; PTO-892, Cited by the examiner) Murray et. al. notes that, "It is hoped that treatment of the porphyrias at the gene level will become possible. In the meantime, treatment is essentially symptomatic. It is important for patients to avoid drugs that cause induction of cytochrome P450. Ingestion of large amounts of carbohydrates (glucose loading) or administration of hematin (a hydroxide of heme) may repress ALAS1, resulting in diminished production of harmful heme precursors. Patients exhibiting photosensitivity may benefit from administration of β-carotene; this compound appears to lessen production of free radicals, thus diminishing photosensitivity." (Murray et. al. Page 278, Column 1, Paragraph 6 to Column 2, Paragraph 1). Even though Murray et. al. recognizes that porphyria is due to abnormalities in heme production, no mention is made of supplementing heme or any of the other intermediates in the synthetic pathway to correct the deficiencies associated with porphyrias. One or skill in the art will not view that recognizing a deficiency in a biochemical pathway automatically equate to a remedy for a disorder by supplementing intermediates or the final product of that pathway. In the instant application, the applicant asserts an

involvement for uroporphyrin I and uroporphyrin III for a wide variety of diseases as diverse as amyotrophic lateral sclerosis and stroke and the treatment for the same with said heme precursors. It is highly unlikely that such disorders can be treated with the administration of said heme precursors.

As discussed above, deficiencies of enzymes in the heme biosynthetic pathway result in the development of porphyrias. The sequential enzymatic steps take place mainly in the erythropoietic system and the liver. (Lim et. al. Page 285, Column 1, Paragraph 1; PTO-892, Cited by the examiner). Associations between porphyrias and other diseases or precipitating factors have been found in many cases. (Lim et. al. Page 285, Column 1, Paragraph 2). Two of the hepatic porphyrias, aminolevulinate dehydratase (ALA) deficiency porphyria and acute intermittent porphyria (AIP), are associated with elevated heme precursors (ALA and porphobilinogen [PBG]). (Lim et. al. Page 285, Column 1, Paragraph 4 to Column 2, Paragraph 1).

Rooney et. al. reports the similarities between multiple sclerosis and some manifestations of acute porphyria that are probably due to central nervous system dysfunction. (Rooney et. al. Page 195, Column 2, Paragraph 2; PTO-892, Cited by the examiner). Rooney et. al notes that iron deficiency, or an excess of iron is likely to affect heme biosynthesis and precipitate porphyria, and that the initiation of iron supplementation resulted in the alleviation of porphyria and MS-like symptoms. (Page 195, Column 1, Paragraph 3). Rooney et. al. further notes that, "A multidisciplinary approach is needed to investigate our hypothesis that the MS phenotype in a subgroup of patients is related to iron

deficiency during heme synthesis causing CNS damage and/or triggering an immune response. Future studies may lead to a clearer definition of disease mechanisms, improved management of MS and ultimately, the development of novel therapy to treat this major cause of nuerologic disability." This study, however, did not show the effect of uroporphyrin intake in patients. However, the symptoms were alleviated by iron supplements. Clearly, a multidisciplinary approach is needed to investigate the effectiveness of uroporphyrin for the treatment of any disease much less the wide variety of diseases the applicant contemplate treating using uroporphyrin. Such effort will involve substantial intellectual input and experimentation by a variety of experienced scientists and clinicians. As such, undue experimentation is necessary to practice the invention as claimed.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses many pathological conditions, which are known to be involved in various, many possible, and different, separate and independent pathology, etiologies, or symptoms.

The skilled artisan would view neurological disorders as a group of maladies not treatable with one medicament or therapeutic regimen. Thus, the skilled artisan

would view that the treatment of different types of neurological disorders by administering uroporphyrins highly unpredictable.

The amount of direction or guidance presented:

The specification provides a description of the heme synthesis pathway in normal individuals and the heme synthesis pathway for a newly defined disease hereditary biochemical multiple sclerosis (HBMS). The applicant notes that, "The above described drawings illustrate the background information necessary to understand the unique and previously unrecognized value of uroporphyrin(ogen) I (URO I), its position in the flow of heme synthesis, and its comparative molecular size in relation to the other pertinent molecules involved in hepatic heme synthesis." The applicant further notes that, "The background information details why URO I, whose importance as a neuroprotector had not previously been recognized, is actually vital to healthy CNS function." However, there is no guidance as to how the administration of any particular uroporphyrins will be effective in treating any of the diseases as claimed.

The presence or absence of working examples:

There are no examples provided. There are no experimental evidence provided showing the effectiveness of uroporphyrins for the treatment of any diseases as claimed.

The lack of working examples is a critical and crucial factor to be considered, especially in cases involving an unpredicatable and undeveloped art. See MPEP § 2164.

The quantity of experimentation necessary:

As discussed above, a multidisciplinary approach is needed to investigate the effectiveness of uroporphyrin isomers for the treatment of the wide variety of diseases the applicant contemplate treating. Such effort will involve substantial intellectual input and experimentation by a variety of experienced scientists and clinicians. As such, undue experimentation is necessary to practice the invention as claimed.

Genetech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, especially the breadth of the claims, the unpredictability of the art, and the lack of guidance or working examples, Applicant fail to provide information sufficient to practice the claimed invention for the prevention of diseases claimed herein absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 recites the phrase "any of several methods." This phrase is not clearly defined in the specification. As such, one of ordinary skill in the art will not be apprised of the metes and bounds of the claimed invention.

Claims 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The use of the acronym BBB renders the claim indefinite. Claim refers to the acronym BBB without defining it first within claims. Where a trademark or trade or abbreviation name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C 112, second paragraph. See *Ex parte Simpson,* 218 USPQ (Bd. App. 1982). The claim scope is uncertain since the abbreviation or trademark or trade name cannot be used to identify any particular material or product. An abbreviation or trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, an abbreviation or trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the abbreviation is used to identify blood brain barrier and accordingly the identification /description is indefinite.

Conclusion

No claim is allowed.

An examination of this application reveals that applicant is unfamiliar with patent prosecution procedure. While an inventor may prosecute the application, lack of skill in this field usually acts as a liability in affording the maximum protection for the invention disclosed. Applicant is advised to secure the services of a registered patent attorney or agent to prosecute the application, since the value of a patent is largely dependent upon skilled preparation and prosecution. The Office cannot aid in selecting an attorney or agent.

A listing of registered patent attorneys and agents is available on the USPTO Internet web site http://www.uspto.gov in the Site Index under "Attorney and Agent Roster." Applicants may also obtain a list of registered patent attorneys and agents located in their area by writing to the Mail Stop OED, Director of the U. S. Patent and Trademark Office, PO Box 1450, Alexandria, VA 22313-1450

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

11/13/06

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